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Substitute for form 1449A/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number	09/993,647
		Filing Date	November 27, 2001
		First Named Inventor	Bernd Riedl et al.
		Group Art Unit	1624
		Examiner Name	Deepak R. Rao
Sheet 1 of 9	Attorney Docket Number	BAYER-0018-A	

U.S. PATENT DOCUMENTS						
Examiner Initials *	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
/DR/		5,559,137		ADAMS	09/24/1996	
↓		6,310,068		BOTTCHER	10/30/2001	
		6,525,046		CIRILLO	02/25/2003	
		6,500,863		JIN	12/31/2002	

FOREIGN PATENT DOCUMENTS								
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		Office ³	Number ⁴	Kind Code ⁵ (if known)				
/DR/		WO	02/062763	A2	Bayer Corp.	8-15-2002		
↓		WO	02/083628	A1	Boehringer Ingelheim Pharmaceuticals Inc.	10-24-2002		
		WO	02/085857	A2	Bayer Corp.	10-31-2002		
		WO	02/085859	A1	Bayer Corp.	10-31-2002		
		WO	97/09973		The Regents Of The University Of California	3-20-1997		
		WO	99/32111		Bayer	07/1999		
		WO	00/56331		Vertex	09/2000		
		WO	03/099771		Novartis	12/2003		
↓		EP	0709225		Nippon	01/1996		

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OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS			
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/DR/		Blanco, "p38 MAPK signaling cascades: ancient roles and new functions," Bioassays, 22:637-645, 2000	
		Dumas, J. "Protein Kinase Inhibitors from the urea class," Curr. Opin. In Drug Discovery and Dev., 5:718-727, 2002	
		Hotte et al., "Bay 43-9006: Early clinical data in patients with advanced solid malignancies," Current Pharmaceutical Design, 8:2249-2253, 2002	
		Kubo et al. "Synthesis and structure-activity relationship of quinazoline-urea derivatives as novel orally active VEGF receptor tyrosine kinase selective inhibitors," Proceedings of the American Association of Cancer Res. 43:182, 2002	
		Madwed et al., "Pharmacological Evaluation of BIRB 796, a selective inhibitor of P38 MAP kinase (MAPK), in animal models of endotoxic shock, inflammation and arthritis," Inflammation Res., 50:S184, 2001	
		Regan et al., "Pyrazole urea-based inhibitors of P38 MAP kinase: from lead compound to clinical candidate," J. Med. Chem. 45:2994-3008, 2002	
		Christopher A. Carter et al., Proceedings of the American Association for Cancer Research - Volume 42 - March 2001 - #4954 Anti-Tumor Efficacy of the Orally Active Raf Kinase Inhibitor BAY 43-9006 in Human Tumor Xenograft Models. , Bayer Corporation.	
		Garcia-Lopes et al., "New routes for the synthesis of pyrrolo(3,2-d)- and (2,3-d)-pyrimidine systems starting from a common pyrrole derivative," Jour. Chem. Soc., pp. 483-487, 1978	
		Facts and Comparisons, 1994, 2703-2705	
		XP-002086152 Gunnar J. Hanson "Pulmonary-Allergy, Dermatological, Gastrointestinal & Arthritis: Inhibitors of p38 kinase," <i>Expert Opinion on Therapeutic Patents</i> , July 1997, vol. 7, no. 7, pp. 729-733(5)	
		T. Murata et al., "Facile synthesis of new pyrrolo[3,4-d]pyrimidine-2,4-diones", Chemical and Pharmaceutical Bulletin, Vol. 22, 1974, pp. 1212-13 (XP-000973679)	
↓		Wilson, Keith et al., "The structural basis for the specificity of pyrimidinylimidazole inhibitors of p38 MAP Kinase" XP-002103155	

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/DR/ ↓		Lowinger, T. B.; Riedl, B.; Wood, J.; Dumas, J.; Smith, R. A.; Khire, U.; Bankston, D.; Monahan, M.K.; Scott, W. J.; Lee, W.; Johnson, J. S.; Caringal, Y.; Turner, T.; Gane, T.; Kennure, N.; Barbosa, J. "Discovery of a Novel Class of Potent Raf Kinase inhibitors: Structure Activity Relationships" Clin. Cancer Res. 2000, 6(suppl.) 335.	
		Redman, A. M.; Johnson, J. S.; Dally, R.; Swartz, S.; Wild, H.; Paulsen, H.; Caringal, Y.; Gunn, D.; Renick, J.; Osterhout, M.; Kingery-Wood, J.; Smith, R. A.; Lee, W.; Dumas, J.; Wilhelm, S. M.; Housley, T. J.; Bhargava, A.; Ranges, G. E.; Shrikhande, A.; Young, D.; Bombara, M.; Scott W. J. "P38 Kinase Inhibitors for the Treatment of Arthritis and Osteoporosis: Thienyl, Furyl and Pyrrolyl Ureas" Bioorg. Med. Chem. Lett. 2001, 11 (1), 9.	
		Dumas, J.; Hatoum-Mokdad, H.; Sibley, R. N.; Smith, R. A.; Scott, W. J.; Khire, U.; Lee, W.; Wood, J.; Wolanin, D.; Cooley, J.; Bankston, D.; Redman, A. M.; Schoenleber, R.; Caringal, Y.; Gunn, D.; Romero, R.; Osterhout, M.; Paulsen, H.; Housley, T. J.; Wilhelm, S. M.; Bhargava, A.; Pirro, J.; Chien, D.-S.; Ranges, G. E.; Shrikhande, A.; Muzsi, A.; Bortolon, E.; Wakefield, J.; Gianpaolo-Ostravage, C.; Chau, T. "Synthesis and Pharmacological Characterization of a Potent, Orally Active p38 Kinase Inhibitor" Bioorg. Med. Chem. Lett. 2002, 12, 1559.	
		Ravi et al., "Activated Raf-1 Causes Growth Arrest in Human Small Cell Lung Cancer Cells," J. Clin. Invest., Vol. 101, No. 1, January 1998, 153-159	
		Nicholas R. Lemoine, "Overview of ras oncogenes and their clinical potential," pp. 85-91	
		Nickel et al., "Carboxylic acid analogues of suramin, potential filaricides," Indian Journal of Chemistry, Vol. 30B, February 1991, p. 182-187	
		Campbell et al., "Increasing complexity of Ras signaling," Oncogene, (1998) 17, 1395-1413	
		Moelling et al., "Signal transduction as target of gene therapy," Institute of Medical Virology, University of Zürich, Recent Results in Cancer Research, Vol. 142, pp. 63-71	
		Stein et al., Internal Medicine, 4th Edition, 1994, pp. 699-715	
	A1	Danson et al., "Improving outcomes in advanced malignant melanoma," Drugs, 2005, 65(6):733-743	

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/DR/		Lowinger, T. B.; Riedl, B.; Dumas, J.; Smith, R. A. "Design and Discovery of Small Molecules Targeting Raf-1 Kinase" Curr. Pharm. Design 2002, 8 (25), 2269.	
		Bankston, D.; Dumas, J.; Natero, R.; Riedl, B.; Monahan, M.-K.; Sibley, R. "A Scaleable Synthesis of BAY 43-9006: A Potent Raf Kinase Inhibitor for the Treatment of Cancer" Org. Proc. Res. Dev. 2002, 6(6), 777-781.	
		Khire, U.; Bankston, D.; Barbosa, J.; Brittelli, D.; Caringal, Y.; Carlson, R.; Dumas, J.; Gane, T.; Heald, S.; Hibner, B.; Johnson, J. S.; Katz, M. E.; Kennure, N.; Kingery-Wood, J.; Lee, W.; Liu, X.-G.; Lowinger, T. B.; Renick, J.; McAlexander, I.; Monahan, M.-K.; Natero, R.; Riedl, B.; Rong, H.; Sibley, R. N.; Smith, R. A.; Wolanin, D.: "Omega-Carboxypyridyl Substituted Ureas as Raf Kinase Inhibitors: SAR of the Amide Substituent" Bioorg. Med. Chem. Lett. 2004, 14, 783-786.	
		Dumas, J.; Smith, R. A.; Lowinger, T. B.: "Recent Developments in the Discovery of Protein Kinase Inhibitors from the Urea Class" Curr. Opin. Drug Discov. Dev. 2004, 7(5), 600-616.	
		Wan PTC, Garnett MJ, Roe SM, Lee S, Niculescu-Duvaz D, Good VM, Cancer genome project, Jones CM, Marshall CJ, Springer CJ, Barford D, Marais R: Mechanism of activation of the RAF-ERK signaling pathway by oncogenic mutations of B-RAF. Cell 2004, 116, 855-867.	
		Mross K, Steinbild S, Baas F, Reil M, Buss P, Mersmann S, Voliotis D, Schwartz B, Brendel E: "Drug-drug interaction pharmacokinetic study with the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors" Int. J. Clin. Pharm. Ther. 2003, 41(12), 618-619.	
		Siu LL, Awada A, Takimoto CH, Moore MJ, Piccart M, Fiander W, Lathia C, Petrensiuc O: "Phase I study of oral Raf-1 kinase inhibitor BAY 43-9006 in combination with gemcitabine in patients with advanced solid tumors" 39th ASCO meeting, Chicago, IL (2003) Abstract 828.	

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/DR/		Richly H, Kupsch P, Passage K, Grugert M, Hilger RA, Kredke S, Voliotis D, Scheulen ME, Seeber S, Strumberg D: "A Phase I clinical and pharmacokinetic study of the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors" Int. J. Clin. Pharm. Ther. 2003, 41(12), 620-621.	
		Sorbera LA, Castaner J, Bozzo J, Leeson PA: "Oncolytic Raf kinase inhibitor" Drugs Future 2002, 27, 1141-1147.	
		Bollag G, Freeman S, Lyons JF, Post LE: "Raf pathway inhibitors in oncology" Curr. Opin. Invest. Drugs 2003, 4(12), 1436-1441.	
		Lee JT, McCubrey JA: BAY-43-9006 (Bayer/Onyx). Curr Opin Invest Drugs (2003) 4(6):757-763.	
		DeGrendele H: "Activity of the Raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors" Clin. Colorectal Cancer 2003, 3(1), 16-18.	
		Wilhelm, S. M.; Carter, C.; Tang, L. Y.; Wilkie, D.; McNabola, A.; Rong, H.; Chen, C.; Zhang, X.; Vincent, P.; McHugh, M.; Cao, Y.; Shujath, J.; Gawlak, S.; Eveleigh, D.; Rowley, B.; Liu, L.; Adnane, L.; Lynch, M.; Auclair, D.; Taylor, I.; Gedrich, R.; Voznesensky, A.; Riedl, B.; Post, L. E.; Bollag, G.; Trail, P.A. "BAY 43-9006 exhibits broad spectrum oral antitumor activity and targets the RAF/MEK/ERK pathway and receptor tyrosine kinases involved in tumor progression and angiogenesis" Cancer Res. 2004, 64(19), 7099-7109.	
		Dumas, J.; Sibley, R.; Riedl, B.; Monahan, M.-K.; Lee, W.; Lowinger, T. B.; Redman, A. M.; Johnson, J. S.; Kingery-Wood, J.; Scott, W. J.; Smith, R. A.; Bobko, M.; Schoenleber, R.; Ranges, G. E.; Housley, T. J.; Bhargava, A.; Wilhelm, S. M.; Shrikhande, A. "Discovery of a New Class of p38 Kinase Inhibitors" Bioorg. Med. Chem. Lett. 2000, 10 (18), 2047.	
↓		Scott McClelland Wilhelm et al., Proceedings of the American Association for Cancer Research - Volume 42 - March 2001 - #4957 A Novel Diphenylurea Raf-1 Kinase Inhibitor (RKI) Blocks the Raf/Mek/Erk Pathway in Tumor Cells. , Bayer Corporation.	

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/DR/		Kempter et al., "Synthese potentieller Pflanzenschutz- und Schädlingsbekämpfungsmittel aus substituierten Anilinen," Pädagogische Hochschule, Eingegangen am 1.7.1982, 101-120	
		Lyons et al., "Discovery of a novel Raf kinase inhibitor," <i>Endocrine-Related Cancer</i> , (2001) 8, 219-225	
		Smith, et al., "Discovery of heterocyclic ureas as a new class of raf kinase inhibitors: identification of a second generation lead by a combinatorial chemistry approach." <i>Bioorganic & Medicinal Chemistry Letters</i> , 11 (2001) 2775-2778	
		Strumberg et al., "Results of phase I pharmacokinetic and pharmacodynamic studies of the raf kinase inhibitor BAY 43-9006 in patients with solid tumors," <i>International Journal of Clinical Pharmacology and Therapeutics</i> , Vol. 40, No. 12/2002 (580-581)	
		Chang et al., "BAY 43-9006 (Sorafenib) inhibitors ectopic (s.c.) and orthotopic growth of a murine model of renal adenocarcinoma (Renca) predominantly through inhibition of tumor angiogenesis," 96 th Annual Meeting, April 16-20, 2005, Anaheim/Orange County, CA	
		Panka et al., "BAY 43-9006 induces apoptosis in melanoma cell lines," 96 th Annual Meeting, April 16-20, 2005, Anaheim/Orange County, CA	
		Auclair, et al., "BAY 43-9006 (Sorafenib) is a potent inhibitor of FLT3 tyrosine kinase signaling and proliferation in AML cells," 96 th Annual Meeting, April 16-20, 2005, Anaheim/Orange County, CA	
		Murphy et al., "BAY 43-9006 controls tumor growth through inhibition of vascular development," 96 th Annual Meeting, April 16-20, 2005, Anaheim/Orange County, CA	
		Spronsen et al., "Novel treatment strategies in clear-cell metastatic renal cell carcinoma," <i>Anti-Cancer Drugs</i> , 2005, 16:709-717	
		Thaimattam et al., "3D-QSAR CoMFA, CoMSIA studies on substituted ureas as Raf-1 kinase inhibitors and its confirmation with structure-based studies," <i>Bioorganic & Medicinal Chemistry</i> , 12(2004) 6415-6425	
		Heim et al., "Antitumor effect and potentiation or reduction in cytotoxic drug activity in human colon carcinoma cells by the Raf kinase inhibitor (RKI) BAY 43-9006," <i>International Journal of Clinical Pharmacology and Therapeutics</i> , Vol. 41, No. 12/2003 (616-617)	

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/DR/		Richly et al., "Results of a phase I trial of BAY 43-9006 in combination with doxorubicin in patients with primary hepatic cancer," <i>International Journal of Clinical Pharmacology and Therapeutics</i> , Vol. 42, No. 11/204 (650-651)	
		Hubbard, "Oncogenic mutations in B-Raf: some losses yield gains," Skirball Institute of Biomolecular Medicine and Department of Pharmacology, New York University School of Medicine, New York, NY	
		Thompson et al., "Recent progress in targeting the Raf/MEK/ERK pathway with inhibitors in cancer drug discovery," <i>Curr. Opin. Pharmacol.</i> , 2005 Aug., 5(4):350-6	
		Moore et al., "Phase I study to determine the safety and pharmacokinetics of the novel Raf kinase and VEGFR inhibitor BAY 43-9006, administered for 28 days on/7 days off in patients with advanced, refractory solid tumors," <i>Annals of Oncology</i> , 16:1688-1694, 2005	
		Ahmad et al., "Kinase inhibition with BAY 43-9006 in renal cell carcinoma," <i>Clinical Cancer Research</i> , Vol. 10, 6388s-6392s, 15 Sept. 2004	
		Strumberg et al., "Phase I clinical and pharmacokinetic study of the novel raf kinase and vascular endothelial growth factor receptor inhibitor BAY 43-9006 in patients with advanced refractory solid tumors," <i>Journal of Clinical Oncology</i> , Vol. 23, No. 5, 10 Feb. 2005, 965-972	
		Clark et al., "Safety and pharmacokinetics of the dual action raf kinase and vascular endothelial growth factor receptor inhibitor, BAY 43-9006, in patients with advanced, refractory solid tumors," <i>Clin. Cancer Res.</i> , 2005:11(15), 1 August 2005, 5472-5480	
		Wilhelm et al., "BAY 43-9006: preclinical data," <i>Curr Pharm Des</i> , 2002, 8(25):2255-7	
✓		Wissner et al., "Analogues of platelet activating factor. 7. Bis-aryl amide and bis-aryl urea receptor antagonists of PAF," <i>J. Med. Chem.</i> , 1992, 35, 4779-4789	

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Application Number	09/993,647
Filing Date	November 27, 2001
First Named Inventor	Bernd Riedl et al.
Group Art Unit	1624
Examiner Name	Deepak R. Rao
Attorney Docket Number	BAYER-0018-A

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

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/DR/		Escudier et al., "Randomized phase III trial of the raf kinase and VEGFR inhibitor sorafenib (BAY 43-9006) in patients with advanced renal cell carcinoma (RCC)," Meeting: 2005 ASCO Annual Meeting, Category: Genitourinary Cancer, Subcategory: Kidney Cancer, Abstract No. 4510	
		Eisen et al., "Phase I trial of BAY 43-9006 (sorafenib) combined with dacarbazine (DTIC) in metastatic melanoma patients," Meeting: 2005 ASCO Annual Meeting, Category: Melamona, Subcategory: Melamona, Abstract No. 7508	
		Adjei et al., "A phase I study of BAY 43-9006 and gefitinib in patients with refractory or recurrent non-small-cell lung cancer (NSCLC)," Meeting: 2005 ASCO Annual Meeting, Category: Developmental Therapeutics: Molecular Therapeutics, Subcategory: Antiangiogenic or Antimetastatic agents, Abstract No. 4510	
		Eisenhauer et al., "Impact of new non-cytotoxics in the treatment in ovarian cancer," <i>Int. J. Gynecol Cancer</i> , 2001, 11 (Suppl. 1), 68-72	
		Strumberg et al., "Phase I and pharmacokinetic study of the raf kinase inhibitor bay 43-9006 in patients with locally advanced or metastatic cancer," #2921, XP-001145481	
		Riedl et al., "Potent raf kinase inhibitors from the diphenylurea class: structure activity relationships," #4956, XP-001145518	
		Iwade et al., "Intra-arterial ACNU, CDDP chemotherapy for brain metastases from lung cancer: comparison of cases with and without intra-arterial mannitol infusion," Dept of Neurological Surgery, Chiba Cancer Center Hospital, Clinical Trial, Journal Article, Randomized Controlled Trial, Vol. 21, No. 6, 513-518 (1993)	
		Geiger et al., "Antitumor activity of a C-raf antisense oligonucleotide in combination with standard chemotherapeutic agents against various human tumors transplanted subcutaneously into nude mice," <i>Clinical Cancer Research</i> , Vol. 3, 1179-1185, July 1997	
		Cunningham et al., "A phase I trial of H-ras antisense oligonucleotide ISIS 2503 administered as a continuous intravenous infusion in patients with advanced carcinoma," <i>Cancer</i> , September 2001, Vol. 92, No. 5, 1265-1271	
✓		Wright et al., "Clinical trials referral resource. Current clinical trials of BAY 43-9006, Part 1," <i>Oncology</i> , 2005 Apr, 19(4):499-502	

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/DR/		Wild, Hanno, "Substructure #1," pp/ 1-150, 1996	
		Wild, Hanno, "Substructure #2," pp/ 1-7, 1996	
		Wild, Hanno, "Substructure #3," pp/ 1-15, 1996	
		Wild, Hanno, "Substructure #4," pp/ 1-107, 1996	
		Wild, Hanno, "Substructure #1," pp/ 1-32, 1996	

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/DR/	2	Phase II Study of Sorafenib in Patients With Advanced Hepatocellular Carcinoma, Ghassan K. Abou-Alfa et al., Journal of Clinical Oncology, Vol. 24, No. 26, pp. 4293-4300. September 10, 2003	
	3	Sorafenib in advanced melanoma: a Phase II randomized discontinuation trial analysis, T. Eisen et al., British Journal of Cancer (2006) pp. 581-586	
	4	Randomized Discontinuation Trial of Sorafenib (BAY 43-9006) Lokesh Jain et al., Cancer Biology & Therapy, pp. 1270-1272, October 2006	
	5	Phase II Placebo-Controlled Randomized Discontinuation Trial of Sorafenib in Patients With Metastatic Renal Cell Carcinoma, Mark J. Ratain et al., Journal of Clinical Oncology, Vol. 24, No. 16, pp. 2505-2510	
	6	Sorafenib and Sunitinib in the Treatment of Advanced Non-Small Cell Lung Cancer, Cesare Gridelli et al., The Oncologist Lung Cancer, pp. 191-200	
	7	First and second generation antisense oligonucleotide inhibitors targeted against human c-raf kinase, Brett P. Monia, Isis Pharmaceuticals Inc., pp. 107-123	
	8	Phase I Evaluation of ISIS 3521, an Antisense Oligodeoxynucleotide to Protein Kinase C-Alpha in Patients With Advanced Cancer, J. Nemunaitis et al., Journal of Clinical Oncology, Vol. 17, No. 11, November 1999, pp. 3586-3595	
	9	Phase I Trial of C-raf Antisense Oligonucleotide ISIS 5132 (CGP 69846A) By 21-Day Continuous Intravenous Infusion (CIV) in Patients with Advanced Cancer (meeting abstract), American Society of Clinical Oncology, 1998 ASCO Annual Meeting, J. Holmlund et al.	
	10	Phase II trial of sorafenib combined with dacarbazine in metastatic melanoma patients, Lorigan, P., et al., ASCO 2006 DTIC (abstract final draft) Jan. 11, 2006.	
	11	Phase II Trial of Single-Agent Sorafenib in Patients with Advanced Non-Small-Cell ung Carcinoma, Gatzemeier, U., et al., ASCO 2006 100557 (abstract draft 3) Jan 4, 2006.	
	12	"First- and second-generation antisense oligonucleotide inhibitors targeted against human c-raf kinase." Ciba Found Symp. 1997; 209:107-19; discussion 119-23.	
	13	"Phase II Trial of Second Antisense Cancer Drug Begins"; NewsRX Purchased Internet Articles, Antisense Technology (clinical trial).	
	14	"Phase I Trial of ISIS 5132, an Antisense Oligonucleotide Inhibitor of c-raf-1, Administered by 24-hour Weekly Infusion to Patients with Advanced Cancer.", Rudin, Charles M., et al., Clinical Cancer Research, Vol. 7, 1214-1220, May 2001.	

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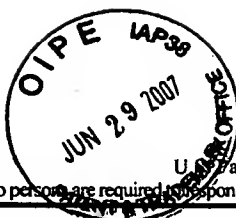
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/DR/	1	<u>Richly H, Henning BF, Kupsch P, Passarge K, Grubert M, Hilger RA, Christensen O, Brendel E, Schwartz B, Ludwig M, Flashar C, Voigtmann R, Scheulen ME, Seeber S, Strumberg D. Results of a Phase I trial of sorafenib (BAY 43-9006) in combination with doxorubicin in patients with refractory solid tumors. +Ann Oncol. 2006 May;17(5):866-73. Epub 2006 Feb 24.</u>	
	2	<u>Moore M, Hirte HW, Siu L, Oza A, Horie SJ, Petrenciuc O, Cihon F, Lathia C, Schwartz B. Phase I study to determine the safety and pharmacokinetics of the novel Raf kinase and VEGFR inhibitor BAY 43-9006, administered for 28 days on/7 days off in patients with advanced, refractory solid tumors. Ann Oncol. 2005 Oct;16(10):1688-94. Epub 2005 Jul 8</u>	
	3	<u>Eisen T, Ahmad T, Flaherty KT, Gore M, Kaye S, Marais R, Gibbens I, Hackett S, James M, Schuchter LM, Nathanson KL, Xia C, Simantov R, Schwartz B, Poulin-Costello M, O'Dwyer PJ, Ratain MJ. Sorafenib in advanced melanoma: a Phase II randomised discontinuation trial analysis. Br J Cancer. 2006 Sep 4;95(5):581-6. Epub 2006 Aug 1.</u>	
	4	<u>Awada A, Hendlisz A, Gil T, Bartholomeus S, Mano M, de Valeriola D, Strumberg D, Brendel E, Haase CG, Schwartz B, Piccart M. Phase I safety and pharmacokinetics of BAY 43-9006 administered for 21 days on/7 days off in patients with advanced, refractory solid tumours. Br J Cancer. 2005 May 23;92(10):1855-61.</u>	
	5	<u>Jain L, Venitz J, Figg WD. Randomized discontinuation trial of sorafenib (BAY 43-9006). Cancer Biol Ther. 2006 Oct;5(10):1270-2. Epub 2006 Oct 16.</u>	
	6	<u>Siu LL, Awada A, Takimoto CH, Piccart M, Schwartz B, Giannaris T, Lathia C, Petrenciuc O, Moore MJ. Phase I trial of sorafenib and gemcitabine in advanced solid tumors with an expanded cohort in advanced pancreatic cancer. Clin Cancer Res. 2006 Jan 1;12(1):144-51.</u>	
	7	<u>Clark JW, Eder JP, Ryan D, Lathia C, Lenz HJ. Safety and pharmacokinetics of the dual action Raf kinase and vascular endothelial growth factor receptor inhibitor, BAY 43-9006, in patients with advanced, refractory solid tumors. Clin Cancer Res. 2005 Aug 1;11(15):5472-80.</u>	
	8	<u>Ahmad T, Eisen T. Kinase inhibition with BAY 43-9006 in renal cell carcinoma. Clin Cancer Res. 2004 Sep 15;10(18 Pt 2):6388S-92S.</u>	
	9	<u>Kupsch P, Henning BF, Passarge K, Richly H, Wieseemann K, Hilger RA, Scheulen ME, Christensen O, Brendel E, Schwartz B, Hofstra E, Voigtmann R, Seeber S, Strumberg D. Results of a phase I trial of sorafenib (BAY 43-9006) in combination with oxaliplatin in patients with refractory solid tumors, including colorectal cancer. Clin Colorectal Cancer. 2005 Sep;5(3): abstract.</u>	
	10	<u>Tong FK, Chow S, Hedley D. Pharmacodynamic monitoring of BAY 43-9006 (Sorafenib) in phase I clinical trials involving solid tumor and AML/MDS patients, using flow cytometry to monitor activation of the ERK pathway in peripheral blood cells. Cytometry B Clin Cytom. 2006 May;70(3):107-14.</u>	
	11	<u>Mross K, Steinbild S, Baas F, Gmehting D, Radtke M, Voliotis D, Brendel E, Christensen O, Unger C. Results from an in vitro and a clinical/pharmacological phase I study with the combination irinotecan and sorafenib. Eur J Cancer. 2007 Jan;43(1):55-63. Epub 2006 Nov 13.</u>	
	12	<u>Richly H, Kupsch P, Passarge K, Grubert M, Hilger RA, Voigtmann R, Schwartz B, Brendel E, Christensen O, Haase CG, Strumberg D. Results of a phase I trial of BAY 43-9006 in combination with doxorubicin in patients with primary hepatic cancer. Int J Clin Pharmacol Ther. 2004 Nov;42(11):650-1. No abstract available.</u>	
	13	<u>Hilger RA, Kredtke S, Scheulen ME, Seeber S, Strumberg D. Correlation of ERK-phosphorylation and toxicities in patients treated with the Raf kinase inhibitor BAY 43-9006. Int J Clin Pharmacol Ther. 2004 Nov;42(11):648-9. No abstract available.</u>	
	14	<u>Richly H, Kupsch P, Passarge K, Grubert M, Hilger RA, Kredtke S, Voliotis D, Scheulen ME, Seeber S, Strumberg D. A phase I clinical and pharmacokinetic study of the Raf kinase inhibitor (RK1) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors. Int J Clin Pharmacol Ther. 2003 Dec;41(12):620-1. No abstract available.</u>	

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/DR/	15	<u>Mross K, Steinbild S, Baas F, Reil M, Buss P, Mersmann S, Voliotis D, Schwartz B, Brendel E.</u> Drug-drug interaction pharmacokinetic study with the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors. <u>Int J Clin Pharmacol Ther.</u> 2003 Dec;41(12):618-9. No abstract available.
	16	<u>Hilger RA, Diaz-Carballo D, Bauer S, Kredtke S, Scheulen ME, Seeher S, Strumberg D.</u> Circadian rhythm in the regulation of the MAP kinase pathway--pitfall in the determination of surrogate parameters? <u>Int J Clin Pharmacol Ther.</u> 2003 Dec;41(12):614-5. No abstract available.
	17	<u>Strumberg D, Voliotis D, Moeller JG, Hilger RA, Riehly H, Kredtke S, Beling C, Scheulen ME, Seeher S.</u> Results of phase I pharmacokinetic and pharmacodynamic studies of the Raf kinase inhibitor BAY 43-9006 in patients with solid tumors. <u>Int J Clin Pharmacol Ther.</u> 2002 Dec;40(12):580-1. No abstract available.
	18	<u>Hilger RA, Kredtke S, Hedley D, Moeller JG, Bauer RJ, Stellberg W, Seeher S, Scheulen ME, Strumberg D.</u> ERK1/2 phosphorylation: a biomarker analysis within a phase I study with the new Raf kinase inhibitor BAY43-9006. <u>Int J Clin Pharmacol Ther.</u> 2002 Dec;40(12):567-8. No abstract available.
	19	<u>Ahori-Alfa GK, Schwartz L, Ricci S, Amadori D, Santoro A, Figer A, De Greve J, Douillard JY, Lathia C, Schwartz B, Taylor I, Mosevici M, Saltz LB.</u> Phase II study of sorafenib in patients with advanced hepatocellular carcinoma. <u>J Clin Oncol.</u> 2006 Sep 10;24(26):4293-300. Epub 2006 Aug 14.
	20	<u>Ratain MJ, Eisen T, Stadler WM, Flaherty KT, Kaye SB, Rosner GL, Gore M, Desai AA, Patnaik A, Xiong HQ, Rowinsky E, Abhruzzese JL, Xia C, Simantov R, Schwartz B, O'Dwyer PJ.</u> Phase II placebo-controlled randomized discontinuation trial of sorafenib in patients with metastatic renal cell carcinoma. <u>J Clin Oncol.</u> 2006 Jun 1;24(16):2505-12. Epub 2006 Apr 24.
	21	<u>Veronese ML, Mosenkis A, Flaherty KT, Gallagher M, Stevenson JP, Townsend RR, O'Dwyer PJ.</u> Mechanisms of hypertension associated with BAY 43-9006. <u>J Clin Oncol.</u> 2006 Mar 20;24(9):1363-9. Epub 2006 Jan 30.
	22	<u>Strumberg D, Riehly H, Hilger RA, Schleueher N, Korfee S, Tewes M, Faghhi M, Brendel E, Voliotis D, Haase CG, Schwartz B, Awada A, Voigtman R, Scheulen ME, Seeher S.</u> Phase I clinical and pharmacokinetic study of the Novel Raf kinase and vascular endothelial growth factor receptor inhibitor BAY 43-9006 in patients with advanced refractory solid tumors. <u>J Clin Oncol.</u> 2005 Feb 10;23(5):965-72. Epub 2004 Dec 21.
	23	<u>Hanna N.</u> Second-line treatment of non-small cell lung cancer: big targets, small progress; small targets, big progress? <u>J Thorac Oncol.</u> 2006 Nov;1(9):927-8. No abstract available.
	24	<u>Escudier B, Eisen T, Stadler WM, Szczylik C, Oudard S, Siebels M, Negrier S, Chevreau C, Sotaka E, Desai AA, Rolland F, Demkow T, Hutson TE, Gore M, Freeman S, Schwartz B, Shan M, Simantov R, Bukowski RM, TARGET Study Group.</u> Sorafenib in advanced clear-cell renal-cell carcinoma. <u>N Engl J Med.</u> 2007 Jan 11;356(2):125-34.
✓	25	Gridelli, Cesare; Maione, Paolo; Del Gaizo, Filomena; Sorafenib an Sunitinib in the Treatment of Advanced Non-Small Cell Lung Cancer; <u>Oncologist</u> 2007; 12; 191-200

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